Please cancel without prejudice claims 1-3, 5, 6, 52 and 55 and amend claims 4, 7, 13, 14, 16, 17, 31, 43, 45-49, 51, 53 and 54. Claims 8-12, 15, 20-30, 35-42, 44 and 50 were withdrawn from further consideration by the Examiner as being drawn to a non-elected invention. The following listing of claims will replace all prior versions and listings of claims in the application.

### **Listing of Claims:**

- 1-3. (Canceled)
- 4. (Currently amended) <u>AThe</u> compound <u>having according to claim 1, 2 or 3 having</u> a formula selected from

$$V-(W-)_{w}(X-)_{x}C((A-)_{a}Z)_{c}$$

$$V-(W-)_{w}(X-)_{x}C(D((A-)_{a}Z)_{d})_{c}$$

$$V-(W-)_w(X-)_xC(D(E((A-)_aZ)_e)_d)_c$$
, and

$$V-(W-)_{w}(X-)_{x}C(D(E(F((A-)_{a}Z)_{f})_{e})_{d})_{c}$$

wherein:

V is selected from [O] and a specifier which is can be removed or transformed by a chemical, photochemical, physical, biological, or enzymatic activation, optionally after prior binding to a receptor, or

taken together, V-B is an oxidized form of B, wherein B is part of C, W or X;

$$(W_{-})_{w}(X_{-})_{x}C((A_{-})_{a})_{e_{7}}$$

$$(W-)_{w}(X-)_{x}C(D((A-)_{a})_{d})_{e}$$

$$(W-)_w(X-)_xC(D(E((A-)_e)_e)_d)_e$$
, and

$$(W_{-})_{w}(X_{-})_{x}C(D(E(F((A_{-})_{e})_{f})_{e})_{d})_{e}$$

independently are self-eliminating multiple release spacers or spacer systems;

Page 3 of 40

<u>each of W and X independently is are each</u> a single release 1,(4+2n) electronic cascade spacer, being the same or different and has the formula:

$$-\mathbf{B} - \mathbf{Q'} - (\mathbf{T} -)_{t}(\mathbf{U} -)_{u}(\mathbf{Y} -)_{y}\mathbf{P}$$

wherein

 $\mathbf{Q}'$  is selected from  $-R^5C=CR^6-$ , S, O,  $NR^5$ ,  $-R^5C=N-$ , and  $-N=CR^5-$ ;

**B** is selected from NR<sup>7</sup>, O, and S;

**P** is  $C(R^3)(R^4)Q$ ;

**Q** has no meaning or is -O-CO-;

t, u, and y are independently an integer of 0 to 5; and

T, U, and Y independently are

$$R^8$$
 or  $R^9$  or  $R^9$  or  $R^9$ 

A is an  $\omega$ -amino aminocarbonyl cyclization elimination spacer;

each of C, D, E, and F independently is are each a self-eliminating multiple release spacer or spacer system that upon activation can maximally release c, d, e, and f leaving groups, respectively, and has the formula:

$$\begin{array}{c|c} \mathbf{G}(\mathbf{P})_g(\mathbf{H}(\mathbf{P})_h(\mathbf{I}(\mathbf{P})_i)_{h'})_{g'} \\ \hline -\mathbf{B} & \mathbf{J}(\mathbf{P})_j(\mathbf{K}(\mathbf{P})_k(\mathbf{L}(\mathbf{P})_l)_{k'})_{j'} \\ \hline \mathbf{M}(\mathbf{P})_m(\mathbf{N}(\mathbf{P})_n(\mathbf{O}(\mathbf{P})_o)_{n'})_{m'} \end{array}$$

wherein

Page 4 of 40

**B** is selected from NR<sup>1</sup>, O, and S;

**P** is  $C(R^2)(R^3)Q-(W-)_w(X-)_x$ ; wherein

**Q** has no meaning or is -O-CO-;

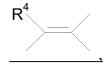
W and X are as defined above;

# G, H, I, J, K, L, M, N, and O independently are:

$$R^4$$
 or  $R^5$  or  $R^5$  or  $R^4$ 

<u>or</u>

# G, J, and M independently are selected from the group of P and hydrogen with the proviso that if two of G, J, and M are hydrogen, the remaining group must be



or be

$$R^4$$
 or  $R^5$  or  $R^5$ 

and at the same time be conjugated to

g, h, i, j, k, l, m, n, o, h', g', k', j', n', m' are independently 0, 1, or 2 with the provisos that

if G = hydrogen or P, g, h, i, h', and g' all equal 0;

Page 5 of 40

if J = hydrogen or P, j, k, l, k', and j' all equal 0;

if M = hydrogen or P, m, n, o, n', and m' all equal 0;

#### if G, H, I, J, K, L, M, N, or O is

$$R^4$$
 or  $R^5$  or  $R^5$ 

then g + g' = 1, h + h' = 1, i = 1, j + j' = 1, k + k' = 1, l = 1, m + m' = 1, n + n' = 1, or o = 1, respectively;

## if G, H, I, J, K, L, M, N, or O is



then g + g' = 2, h + h' = 2, i = 2, j + j' = 2, k + k' = 2, l = 2, m + m' = 2, n + n' = 2, or o = 1, respectively:

if g' = 0 and G is not hydrogen or P, then h, h', and i equal 0 and g > 0;

if g = 0 and G is not hydrogen or P, then g' > 0;

if g' > 0 and h' = 0, then i = 0 and h > 0;

if g' > 0 and h = 0, then h' > 0 and i > 0;

if j' = 0 and **J** is not hydrogen or **P**, then k, k', and I equal 0 and j > 0;

if j = 0 and **J** is not hydrogen or **P**, then j' > 0;

if j' > 0 and k' = 0, then l = 0 and k > 0;

if j' > 0 and k = 0, then k' > 0 and l > 0;

if m' = 0 and M is not hydrogen or P, then n, n', and o equal 0 and m > 0;

if m = 0 and M is not hydrogen or P, then m' > 0;

Page 6 of 40

if m' > 0 and n' = 0, then o = 0 and n > 0;

if m' > 0 and n = 0, then n' > 0 and o > 0;

with the proviso that

if the compound contains only C and no D, no E, and no F are present, and  $B = NR^1$ , and G and M are H, and g, h, i, h', g', k, l, k', l', m, n, o, n', and m' are 0, and  $J = NR^1$ 

, and j = 2, and Q = -O-CO-, and w and x are 0, and  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^4$  are H, then at least one of the **Z** groups is not connected to **Q** via an aliphatic amino group;

wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ , and  $R^9$  independently are selected from H, a  $C_{1-6}$  alkyl group, a  $C_{3-20}$  heterocyclyl group, a  $C_{5-20}$  aryl group, a  $C_{1-6}$  alkoxy group, hydroxy (OH), amino (NH<sub>2</sub>), mono-substituted amino (NR<sub>x</sub>H), disubstituted amino (NR<sub>x</sub><sup>1</sup>R<sub>x</sub><sup>2</sup>), nitro (NO<sub>2</sub>), halogen, CF<sub>3</sub>, CN, CONH<sub>2</sub>, SO<sub>2</sub>Me, CONHMe, a cyclic  $C_{1-5}$  alkylamino group, imidazolyl, a  $C_{1-6}$  alkylpiperazinyl group, morpholino, thiol (SH), thioether (SR<sub>x</sub>), tetrazole, carboxy (COOH), carboxylate (COOR<sub>x</sub>), sulphoxy (S(=O)<sub>2</sub>OH), sulphonate (S(=O)<sub>2</sub>OR<sub>x</sub>), sulphoxyl (S(=O)<sub>2</sub>R<sub>x</sub>), sulphinyl (S(=O)R<sub>x</sub>), phosphonooxyl (OP(=O)(OH)<sub>2</sub>), and phosphate (OP(=O)(OR<sub>x</sub>)<sub>2</sub>), wherein  $R_x$ ,  $R_x$ <sup>1</sup> and  $R_x$ <sup>2</sup> are independently selected from a  $C_{1-6}$  alkyl group, a  $C_{3-20}$  heterocyclyl group and a  $C_{5-20}$  aryl group, or two or more of the substituents  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ , and  $R^9$  optionally are connected to one another to form one or more aliphatic or aromatic cyclic structures;

each **Z** is independently <u>a therapeutic or diagnostic moiety</u> a leaving group or H or OH or a reactive moiety;

a is 0 or 1;

c, d, e, and f are independently an integer from 2 (included) to 24 (included); w and x are independently an integer from 0 (included) to 5 (included); and

Page 7 of 40

n is an integer of 0 (included) to 10 (included).

5-6. (Canceled)

- 7. (Currently amended) The compound according to claim 4, wherein the <u>Zleaving</u> groups [[Z]] are linked to the self-eliminating multiple release spacer or spacer system via an O, S, or aromatic N of the <u>Zleaving</u> group.
- 8. (Withdrawn) The compound according to claim 4, wherein the leaving groups **Z** are linked to the self-eliminating multiple release spacer or spacer system via an aliphatic N and wherein at least one multiple release spacer or spacer system of either generation **C**, **D** (if present), **E** (if present), or **F** (if present) is a phenol- or thiophenol-based multiple release spacer or spacer system, meaning that
  - i)  $\mathbf{B} = \mathbf{O}$  or S for at least one multiple release spacer in said generation, or
- ii) when  $\mathbf{B} = \mathbf{N}$  for all multiple release spacers in said generation, at least one single release spacer is connected to at least two branches of at least one multiple release spacer in said generation, and  $\mathbf{B} = \mathbf{O}$  or S for at least two of said single release spacers.
- 9. (Withdrawn) The compound according to claim 8, wherein  $\mathbf{B} = \mathbf{O}$  or S for all multiple release spacers or spacer systems in said generation.
- 10. (Withdrawn) The compound according to claim 8, wherein the phenol- or thiophenol-based multiple release spacers are connected to either **A** or **Z** or **S**, wherein **S** has no meaning or is H, OH, or a reactive moiety that allows for coupling the multiple release spacer system to leaving groups **Z** to afford compounds independently selected from:

$$\begin{aligned} \mathbf{V} - (\mathbf{W} -)_{w} (\mathbf{X} -)_{x} \mathbf{C} ((\mathbf{A} -)_{a} \mathbf{Z})_{c}, \\ \\ \mathbf{V} - (\mathbf{W} -)_{w} (\mathbf{X} -)_{x} \mathbf{C} (\mathbf{D} ((\mathbf{A} -)_{a} \mathbf{Z})_{d})_{c}, \\ \\ \mathbf{V} - (\mathbf{W} -)_{w} (\mathbf{X} -)_{x} \mathbf{C} (\mathbf{D} (\mathbf{E} ((\mathbf{A} -)_{a} \mathbf{Z})_{e})_{d})_{c}, \text{ and} \\ \\ \mathbf{V} - (\mathbf{W} -)_{w} (\mathbf{X} -)_{x} \mathbf{C} (\mathbf{D} (\mathbf{E} (\mathbf{F} ((\mathbf{A} -)_{a} \mathbf{Z})_{f})_{e})_{d})_{c}. \end{aligned}$$

Page 8 of 40

11. (Withdrawn) The compound according to claim 4, wherein the cyclization elimination spacer **A** is a compound having the formula:

wherein:

a is an integer of 0 or 1;

b is an integer of 0 or 1;

c is an integer of 0 or 1; provided that

a + b + c = 2 or 3:

 $R^1$  and  $R^2$  independently represent H,  $C_{1-6}$  alkyl, said alkyl being optionally substituted with one or more of the following groups: hydroxy (OH), ether (OR<sub>x</sub>), amino (NH<sub>2</sub>), monosubstituted amino (NR<sub>x</sub>H), di-substituted amino (NR<sub>x</sub> $^1$ R<sub>x</sub> $^2$ ), nitro (NO<sub>2</sub>), halogen, CF<sub>3</sub>, CN, CONH<sub>2</sub>, SO<sub>2</sub>Me, CONHMe, cyclic  $C_{1-5}$  alkylamino, imidazolyl,  $C_{1-6}$  alkylpiperazinyl, morpholino, thiol (SH), thioether (SR<sub>x</sub>), tetrazole, carboxy (COOH), carboxylate (COOR<sub>x</sub>), sulphoxy (S(=O)<sub>2</sub>OH), sulphonate (S(=O)<sub>2</sub>OR<sub>x</sub>), sulphonyl (S(=O)<sub>2</sub>R<sub>x</sub>), sulphixy (S(=O)OH), sulphinate (S(=O)OR<sub>x</sub>), sulphinyl (S(=O)R<sub>x</sub>), phosphonooxy

 $(OP(=O)(OH)_2)$ , and phosphate  $(OP(=O)(OR_x)_2)$ , where  $R_x$ ,  $R_x^{-1}$  and  $R_x^{-2}$  are selected from a  $C_{1-6}$  alkyl group, a  $C_{3-20}$  heterocyclyl group and a  $C_{5-20}$  aryl group; and

 $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ , and  $R^8$  independently represent H,  $C_{1-6}$  alkyl,  $C_{3-20}$  heterocyclyl,  $C_{5-20}$  aryl,  $C_{1-6}$  alkoxy, hydroxy (OH), amino (NH<sub>2</sub>), mono-substituted amino (NR<sub>x</sub>H), disubstituted amino (NR<sub>x</sub><sup>1</sup>R<sub>x</sub><sup>2</sup>), nitro (NO<sub>2</sub>), halogen, CF<sub>3</sub>, CN, CONH<sub>2</sub>, SO<sub>2</sub>Me, CONHMe, cyclic  $C_{1-5}$  alkylamino, imidazolyl,  $C_{1-6}$  alkylpiperazinyl, morpholino, thiol (SH), thioether (SR<sub>x</sub>), tetrazole, carboxy (COOH), carboxylate (COOR<sub>x</sub>), sulphoxy (S(=O)<sub>2</sub>OH), sulphonate (S(=O)<sub>2</sub>OR<sub>x</sub>), sulphonyl (S(=O)<sub>2</sub>R<sub>x</sub>), sulphixy (S(=O)OH), sulphinate (S(=O)OR<sub>x</sub>), sulphinyl (S(=O)R<sub>x</sub>), phosphonooxy (OP(=O)(OH)<sub>2</sub>), or phosphate (OP(=O)(OR<sub>x</sub>)<sub>2</sub>), where  $R_x$ ,  $R_x$ <sup>1</sup> and  $R_x$ <sup>2</sup> are selected from a  $C_{1-6}$  alkyl group, a  $C_{3-20}$  heterocyclyl group and a  $C_{5-20}$  aryl group; or

Page 9 of 40

R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, and R<sup>8</sup> can be a part of one or more aliphatic or aromatic cyclic structures, two or more of the substituents R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, or R<sup>8</sup> optionally being connected to one another to form one or more aliphatic or aromatic cyclic structures.

- 12. (Withdrawn) The compound according to claim 4, wherein group  $\mathbf{A}$  is an  $\omega$ -amino aminocarbonyl cyclization spacer, and  $\mathbf{Z}$  is a moiety coupled via its hydroxyl group to  $\mathbf{A}$ .
- 13. (Currently amended) The compound according to claim 4, wherein <u>in</u>

$$\underline{V}$$
- $(\underline{W}$ - $)_{\underline{w}}(\underline{X}$ - $)_{\underline{x}}\underline{C}(\underline{Z})_{\underline{c}}$ ,

 $V-(W-)_w(X-)_xC(D(Z)_d)_c$ 

 $V-(W-)_w(X-)_xC(D(E(Z)_e)_d)_c$ , and

 $V-(W-)_w(X-)_xC(D(E(F(Z)_f)_e)_d)_c$ 

w + x > 0.

14. (Currently amended) The compound according to claim 4, wherein A compound having a formula selected from

 $V-(W-)_w(X-)_xC(Z)_c$ 

 $V-(W-)_w(X-)_xC(D(Z)_d)_{c_x}$ 

 $V-(W-)_w(X-)_xC(D(E(Z)_e)_d)_c$ , and

 $V-(W-)_w(X-)_xC(D(E(F(Z)_f)_e)_d)_c$ 

wherein:

V is a specifier which can be removed or transformed by a chemical, photochemical, physical, biological, or enzymatic activation, optionally after prior binding to a receptor, or

taken together, V-B is an oxidized form of B, wherein B is part of C, W, or X;

$$(W-)_{w}(X-)_{x}C_{[[c]]},$$

$$(\mathbf{W}-)_{\mathbf{w}}(\mathbf{X}-)_{\mathbf{x}}\mathbf{C}(\mathbf{D}_{\lceil\lceil d\rceil\rceil})_{\mathbf{c}},$$

$$(\mathbf{W}-)_{\mathbf{w}}(\mathbf{X}-)_{\mathbf{x}}\mathbf{C}(\mathbf{D}(\mathbf{E}_{\lceil [\mathbf{e}] \rceil})_{\mathbf{d}})_{\mathbf{c}}$$
 or

# $(W\text{-})_w(X\text{-})_xC(D(E(F_{[[f]]})_e)_d)_c$

is selected from the group consisting of

Page 20 of 40

and from the compounds depicted above wherein single release 1,6-elimination paminobenzyloxycarbonyl spacer(s) are replaced by single release 1,8-elimination paminocinnamyloxycarbonyl spacer(s)

 $R^1 = O \text{ or } OC(O)O$ 

each **Z** is independently a therapeutic or diagnostic moiety; and c, d, e, and f are independently an integer from 2 (included) to 24 (included).

- 15. (Withdrawn) The compound according to claim 14, the compound further comprising cyclization elimination spacers **A**.
- 16. (Currently amended) The compound according to claim [[1]] $\underline{4}$ , wherein the specifier **V** contains a substrate that can be cleaved by plasmin, one of the cathepsins, cathepsin B,  $\beta$ -glucuronidase, prostate-specific antigen (PSA), urokinase-type plasminogen activator (u-PA), a

Page 21 of 40

member of the family of matrix metalloproteinases, or <u>wherein V-B</u>, taken together, wherein the specifier V is [O] or is an oxidized form of B, or V contains a nitro-(hetero)aromatic moiety, that can be removed or transformed by reduction under hypoxic conditions or by reduction by a nitroreductase.

- 17. (Currently amended) The compound according to claim [[1]]4, wherein **Z** is selected from an antibiotic, an anti-inflammatory agent, an anti-viral agent, and preferably an anticancer agent.
- 18. (Previously presented) The compound of claim 17, wherein **Z** is selected from

(hydroxyl containing cytotoxic compounds) etoposide, combrestatin, camptothecin, irinotecan (CPT-11), SN-38, topotecan, 9-aminocamptothecin, 9-nitrocamptothecin, 10-hydroxycamptothecin, GG211, lurtotecan, paclitaxel, docetaxel, esperamycin, 1,8-dihydroxybicyclo[7.3.1]trideca-4-ene-2,6-diyne-13-one, anguidine, doxorubicin, morpholine-doxorubicin, N-(5,5-diacetoxypentyl) doxorubicin, daunorubicin, epirubicin, idarubicin, mitoxantrone, vincristine, vinblastine, tallysomycin, bleomycin, 4-bis(2-chloroethyl)aminophenol, 4-bis(2-fluoroethyl)aminophenol, and derivatives thereof,

(sulfhydryl containing compounds) esperamicin and 6-mercaptopurine, and derivatives thereof,

(carboxyl containing compounds) methotrexate, aminopterin, camptothecin (ringopened form of the lactone), chlorambucil, melphalan, butyric acid and retinoic acid, and derivatives thereof, and

(aziridine amino containing or aromatic amino containing compounds) mitomycin C, mitomycin A, an anthracycline derivative containing an amine functionality with sufficient leaving group ability, mitoxantrone, 9-amino camptothecin, methotrexate, aminopterin, tallysomycin, bleomycin, actinomycin, N,N-bis(2-chloroethyl)-p-phenylenediamine, N,N-bis(2-fluoroethyl)-p-phenylenediamine, deoxycytidine, cytosine arabinoside, gemcitabine, and derivatives thereof, and

Page 22 of 40

(aliphatic amino containing compounds) daunorubicin, doxorubicin, epirubicin, idarubicin, N-(5,5-diacetoxypentyl)doxorubicin, an anthracycline, N<sup>8</sup>-acetyl spermidine, 1-(2-chloroethyl)-1,2-dimethanesulfonyl hydrazine, or derivatives thereof.

- 19. (Previously presented) The compound according to claim 18, wherein **Z** represents paclitaxel, docetaxel, or a derivative thereof, which is coupled to the self-eliminating multiple release spacer or spacer system via its 2'-hydroxyl group.
- 20. (Withdrawn) The compound according to claim 18, wherein **Z** represents camptothecin, irinotecan (CPT-11), SN-38, topotecan, 9-aminocamptothecin, 9-nitrocamptothecin, 10-hydroxycamptothecin, GG211, lurtotecan, or a derivative thereof, which is coupled to the self-eliminating multiple release spacer or spacer system via its 20-hydroxyl group.
- 21. (Withdrawn) The compound according to claim 18, wherein **Z** represents SN-38, topotecan, 10-hydroxycamptothecin, etoposide, 4-bis(2-chloroethyl)aminophenol, 4-bis(2-fluoroethyl)aminophenol, or a derivative thereof, which is coupled to the self-eliminating multiple release spacer or spacer system via its phenolic hydroxyl group.
- 22. (Withdrawn) The compound according to claim 18, wherein **Z** represents 9-aminocamptothecin, N,N-bis(2-chloroethyl)-p-phenylenediamine, N,N-bis(2-fluoroethyl)-p-phenylenediamine, or a derivative thereof, which is coupled to the self-eliminating multiple release spacer or spacer system via its aromatic primary amine group.
- 23. (Withdrawn) The compound according to claim 18, wherein **Z** represents daunorubicin, doxorubicin, epirubicin, idarubicin, N-(5,5-diacetoxypentyl)doxorubicin, an anthracycline, N<sup>8</sup>-acetyl spermidine, 1-(2-chloroethyl)-1,2-dimethanesulfonyl hydrazine, or derivatives thereof, which is coupled to the self-eliminating multiple release spacer or spacer system via its primary aliphatic amino group; wherein

Page 23 of 40

at least one multiple release spacer or spacer system of either generation C, D (if present), E (if present), or F (if present) is a phenol- or thiophenol-based multiple release spacer or spacer system, meaning that

- i)  $\mathbf{B} = \mathbf{O}$  or S for at least one multiple release spacer in said generation, or
- ii) when  $\mathbf{B} = \mathbf{N}$  for all multiple release spacers in said generation, at least one single release spacer is connected to at least two branches of at least one multiple release spacer in said generation, and  $\mathbf{B} = \mathbf{O}$  or S for at least two of said single release spacers.
- 24. (Withdrawn) The compound according to claim 23, wherein  $\mathbf{B} = \mathbf{O}$  or S for all multiple release spacers or spacer systems in said generation.
- 25. (Withdrawn) The compound according to claims 23, wherein the phenol- or thiophenol-based multiple release spacers are connected to either **A** or **Z** or **S**, wherein **S** has no meaning or is H, OH, or a reactive moiety that allows for coupling the multiple release spacer system to leaving groups **Z** to afford compounds independently selected from:

$$\begin{aligned} \mathbf{V}\text{-}(\mathbf{W}\text{-})_w(\mathbf{X}\text{-})_x\mathbf{C}((\mathbf{A}\text{-})_a\mathbf{Z})_c,\\ \\ \mathbf{V}\text{-}(\mathbf{W}\text{-})_w(\mathbf{X}\text{-})_x\mathbf{C}(\mathbf{D}((\mathbf{A}\text{-})_a\mathbf{Z})_d)_c,\\ \\ \mathbf{V}\text{-}(\mathbf{W}\text{-})_w(\mathbf{X}\text{-})_x\mathbf{C}(\mathbf{D}(\mathbf{E}((\mathbf{A}\text{-})_a\mathbf{Z})_e)_d)_c,\text{ and}\\ \\ \mathbf{V}\text{-}(\mathbf{W}\text{-})_w(\mathbf{X}\text{-})_x\mathbf{C}(\mathbf{D}(\mathbf{E}(\mathbf{F}((\mathbf{A}\text{-})_a\mathbf{Z})_f)_e)_d)_c. \end{aligned}$$

26. (Withdrawn) A compound having a formula selected from

$$\begin{aligned} \mathbf{V} - (\mathbf{W} -)_{w} (\mathbf{X} -)_{x} \mathbf{C} ((\mathbf{A} -)_{a} \mathbf{S})_{c}, \\ \mathbf{V} - (\mathbf{W} -)_{w} (\mathbf{X} -)_{x} \mathbf{C} (\mathbf{D} ((\mathbf{A} -)_{a} \mathbf{S})_{d})_{c}, \\ \mathbf{V} - (\mathbf{W} -)_{w} (\mathbf{X} -)_{x} \mathbf{C} (\mathbf{D} (\mathbf{E} ((\mathbf{A} -)_{a} \mathbf{S})_{e})_{d})_{c}, \text{ and} \\ \mathbf{V} - (\mathbf{W} -)_{w} (\mathbf{X} -)_{x} \mathbf{C} (\mathbf{D} (\mathbf{E} (\mathbf{F} ((\mathbf{A} -)_{a} \mathbf{S})_{f})_{e})_{d})_{c}, \\ \end{aligned}$$
wherein:

Page 24 of 40

V is selected from [O] and a specifier which is removed or transformed by a chemical, photochemical, physical, biological, or enzymatic activation, optionally after prior binding to a receptor;

$$\begin{split} &(\mathbf{W}\text{-})_w(\mathbf{X}\text{-})_x\mathbf{C}((\mathbf{A}\text{-})_a)_c,\\ &(\mathbf{W}\text{-})_w(\mathbf{X}\text{-})_x\mathbf{C}(\mathbf{D}((\mathbf{A}\text{-})_a)_d)_c,\\ &(\mathbf{W}\text{-})_w(\mathbf{X}\text{-})_x\mathbf{C}(\mathbf{D}(\mathbf{E}((\mathbf{A}\text{-})_a)_e)_d)_c, \text{ and}\\ &(\mathbf{W}\text{-})_w(\mathbf{X}\text{-})_x\mathbf{C}(\mathbf{D}(\mathbf{E}(\mathbf{F}((\mathbf{A}\text{-})_a)_f)_e)_d)_c \end{split}$$

independently are self-eliminating multiple release spacers or spacer systems;

W and X are each a single release 1,(4+2n) electronic cascade spacer, being the same or different;

A is a cyclization elimination spacer;

C, D, E, and F independently are a self-eliminating multiple release spacer or spacer system that upon activation can maximally release c, d, e, and f leaving groups, respectively;

a is 0 or 1;

c, d, e, and f are independently an integer from 2 (included) to 24 (included);

w and x are independently an integer from 0 (included) to 5 (included);

n is an integer of 0 (included) to 10 (included);

each S independently has no meaning or is H, OH, or a reactive moiety that allows for coupling the multiple release spacer system to leaving groups Z, which may be the same or different, to afford compounds

$$\begin{aligned} \mathbf{V} - (\mathbf{W} -)_{w} (\mathbf{X} -)_{x} \mathbf{C} ((\mathbf{A} -)_{a} \mathbf{Z})_{c}, \\ \\ \mathbf{V} - (\mathbf{W} -)_{w} (\mathbf{X} -)_{x} \mathbf{C} (\mathbf{D} ((\mathbf{A} -)_{a} \mathbf{Z})_{d})_{c}, \\ \\ \mathbf{V} - (\mathbf{W} -)_{w} (\mathbf{X} -)_{x} \mathbf{C} (\mathbf{D} (\mathbf{E} ((\mathbf{A} -)_{a} \mathbf{Z})_{e})_{d})_{c}, \text{ and} \\ \\ \mathbf{V} - (\mathbf{W} -)_{w} (\mathbf{X} -)_{x} \mathbf{C} (\mathbf{D} (\mathbf{E} (\mathbf{F} ((\mathbf{A} -)_{a} \mathbf{Z})_{f})_{e})_{d})_{c}, \text{ respectively; and} \end{aligned}$$

Page 25 of 40

each **Z** is independently a leaving group or H or OH or a reactive moiety.

- 27. (Withdrawn) The compound according to claim 26, wherein the reactive moiety **S** is connected via a carbonyl group to the multiple release spacer or spacer system.
- 28. (Withdrawn) The compound according to claim 27, wherein **S** represents *N*-succinimidyl-*N*-oxide, *p*-nitrophenoxide, pentafluorophenoxide, or chloride.
- 29. (Withdrawn) The compound according to claim 26, wherein S is connected to the methylene group of the multiple release spacer or spacer system.
- 30. (Withdrawn) The compound according to claim 29, wherein **S** represents chloride, bromide, *p*-toluenesulfonate, trifluoromethylsulfonate, or methylsulfonate.
- 31. (Currently amended) The compound according to claim [[1]]4, wherein the specifier **V** is a tripeptide.
- 32. (Previously presented) The compound according to claim 31, wherein the tripeptide is linked via its C-terminus to the self-eliminating multiple release spacer or spacer system.
- 33. (Previously presented) The compound of claim 32, wherein the C-terminal amino acid residue of the tripeptide is selected from arginine and lysine, the middle amino acid residue of the tripeptide is selected from alanine, valine, leucine, isoleucine, methionine, phenylalanine, cyclohexylglycine, tryptophan and proline, and the N-terminal amino acid residue of the tripeptide is selected from a D-amino acid residue and a protected L-amino acid residue including protected glycine.
- 34. (Previously presented) The compound according to claim 33, wherein the specifier V is selected from D-alanylphenylalanyllysine, D-valylleucyllysine, D-alanylleucyllysine, D-valylphenylalanyllysine, D-valyltryptophanyllysine and D-alanyltryptophanyllysine.

Page 26 of 40

- 35. (Withdrawn) The compound according to claim 1, wherein the specifier **V** is an amino-terminal capped peptide covalently linked via the C-terminus to the self-eliminating multiple release spacer or spacer system.
- 36. (Withdrawn) The compound according to claim 35, wherein the specifier **V** is selected from benzyloxycarbonylphenylalanyllysine, benzyloxycarbonylvalylcitrulline, tert-butyl phenylalanyllysine, benzyloxycarbonylalanylarginylarginine, benzyloxycarbonylphenylalanyl-N-tosylarginine, 2-aminoethylthiosuccinimidopropionylvalinylcitrulline, 2-aminoethylthiosuccinimidopropionyllysylphenylalanyllysine, acetylphenylalanyllysine, and benzyloxycarbonylphenylalanyl-O-benzoylthreonine.
- 37. (Withdrawn) The compound according to claim 1, wherein the specifier **V** comprises a reactive moiety that can be used to couple said compound to a targeting moiety.
- 38. (Withdrawn) The compound according to claim 37, wherein the reactive moiety is

$$-\bigvee_{0}^{N} \quad \text{or} \quad \bigvee_{0}^{N} \quad \text{or} \quad -s-s-\bigvee_{0}^{N}$$

wherein X is a leaving group.

- 39. (Withdrawn) The compound according to claim 37, wherein the reactive moiety is selected from an *N*-hydroxysuccinimide ester, a *p*-nitrophenyl ester, a pentafluorophenyl ester, an isothiocyanate, an isocyanate, an anhydride, an acid chloride, a sulfonyl chloride, and an aldehyde.
- 40. (Withdrawn) The compound according to claim 37, wherein the reactive moiety is a hydrazine group or an amino group.

Page 27 of 40

- 41. (Withdrawn) The compound according to claim 1, wherein the specifier **V** comprises a targeting moiety.
- 42. (Withdrawn) The compound according to claim 41, wherein the targeting moiety is selected from the group consisting of a protein or protein fragment, an antibody or an antibody fragment, a receptor-binding or peptide vector moiety and a polymeric or dendritic moiety.
- 43. (Currently amended) <u>AThe</u> compound according to claim 1-selected from the group consisting of

Page 29 of 40

$$H_{i,N} = \bigoplus_{i \in \{l_{i},l_{i}\}} \bigoplus_{i \in \{l_$$

Page 34 of 40

$$R^7 = O \text{ or } OC(O)O, \quad R^0 =$$

$$R^{10} OH \text{ and } R^0 = H, \text{ or } R^0 =$$

$$R^{10} OH \text{ and } R^0 = H, \text{ or } R^0 =$$

$$R^{10} OH \text{ and } R^0 = H, \text{ or } R^0 =$$

$$R^{10} OH \text{ and } R^0 = H, \text{ or } R^0 =$$

$$R^{10} OH \text{ and } R^0 = H, \text{ or } R^0 = H,$$

and salts thereof.

44. (Withdrawn) Use of a compound having a formula selected from

$$V-(W-)_w(X-)_xC((A-)_aS)_c$$

$$V-(W-)_w(X-)_xC(D((A-)_aS)_d)_c$$

$$V-(W-)_w(X-)_xC(D(E((A-)_aS)_e)_d)_c$$
, and

$$V-(W-)_w(X-)_xC(D(E(F((A-)_aS)_f)_e)_d)_c,$$

Page 35 of 40

for the preparation of a compound of claim 4;

wherein each S independently has no meaning or is H, OH, or a reactive moiety that allows for coupling the multiple release spacer system to leaving groups Z, which may be the same or different; and

V, W, X, C, D, E, F, A, w, x, c, d, e, f, and a are as defined in claim 4.

- 45. (Currently amended) A diagnostic assay process, the process comprising:

  incubating a sample comprising an enzyme with wherein a compound according to claim [[1]]4 to cause enzymatic cleavage of the compound, and detecting one or more molecules liberated by the enzymatic cleavage is used.
- 46. (Currently amended) The diagnostic assay process according to claim 45, wherein the detection of the one or more molecules determines the presence or amount of thean enzyme is determined.
- 47. (Currently amended) The diagnostic assay process according to claim 46, wherein the detection of the one or more molecules determines the presence or amount of a protease is determined.
- 48. (Currently amended) The diagnostic assay process according to claim 47, wherein the compound that is used comprises a substrate for said protease and <u>one or more leaving group-</u>**Z** groups are is detected.
- 49. (Currently amended) The diagnostic assay process according to claim 47, wherein the compound that is used comprises a substrate for <u>thean</u> enzyme, which is the product of cleavage of its pro-enzyme precursor by said protease and <u>one or more leaving group Z groups are is</u> detected.
- 50. (Withdrawn) A composite structure comprising two or more compounds according to claim 1 connected with a polymeric structure.

Page 36 of 40

- 51. (Currently amended) The compound according to claim [[1]]4, wherein the specifier V can be removed or transformed by an enzyme that is transported to the vicinity of or inside target cells or target tissue via ADEPT, PDEPT, MDEPT, VDEPT, or GDEPT.
- 52. (Canceled)
- 53. (Currently amended) A pharmaceutical composition comprising a compound according to claim [[1]]4.
- 54. (Currently amended) A process for preparing a pharmaceutical composition comprising the step of mixing a compound according to claim [[1]]4 with a pharmaceutically acceptable carrier.
- 55. (Canceled)